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Supplemental Material

The Genetic Architecture of Arsenic Metabolism Efficiency: A SNP-Based Heritability Study of Bangladeshi Adults

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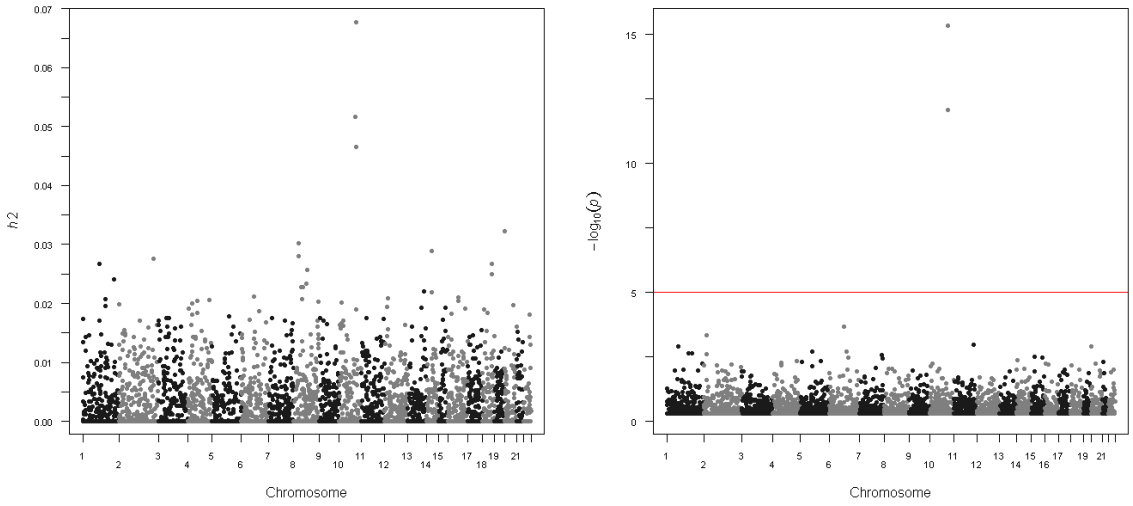
LMM Analysis

The LMM (linear mixed model) includes effects for all measured SNPs: $y=b_0+\sum w_i b_i +e$, where y is the phenotype of interest, b_i is the effect of the i-th SNP only, and w is a standardized genotype: $w_i= (z_i-2p_i)/ \sqrt{2p_i(1 - p_i)}$, where z_i is an individual's minor allele count and p_i is the minor allele frequency, and e is the residual. Assuming Hardy-Weinberg equilibrium, the scaling allows SNP effects (b_i) to be treated as random variables from a distribution with variance σ_b^2. The analysis is implemented in an equivalent model, y= g + e, where g=Wb is a vector of genetic values calculated from an individual's genotype values and the variance of g is $WW'\sigma_b^2$. WW' is a matrix of pair-wise genetic relationships (genetic relationship matrix, GRM). The variance of the effects in vector g is equivalent to the variance explained by all SNPs in the original model that fits the SNP effects directly. This LMM allows us to estimate the overall heritability even though the number of SNPs exceeds the sample size, a situation in which typical linear regression would fail. The LMM was implemented in the Genome-wide Complex Trait Analysis (GCTA) software package (Yang et al. 2011).

Reference

Yang J, Lee SH, Goddard ME, Visscher PM. 2011. GCTA: A tool for genome-wide complex trait analysis. American journal of human genetics 88:76-82.

Figure S1. Regional heritability estimates (A) and corresponding P-values (B) for DMA% based on all samples (n= 2,053). Estimates were obtained using imputed SNP data with window size 300 SNPs with a 50 SNP overlap between windows. 4,787 tests were conducted. Red line indicates Bonferroni-corrected p threshold.



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